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EXAMINER	
GRASER, JENNIFER E	
ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,505	LEMICHEZ ET AL.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 14-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 14-16* is/are rejected.

7)☒ Claim(s) *2,3,5,6 and 14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/15/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112-2nd paragraph

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-11, and 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because it is unclear what is encompassed by the term “Rho GTPase activator”. The mere recitation of a name to describe the invention is not sufficient to satisfy the Statute's requirement of adequately describing and setting forth the inventive concept. The claim should provide any structural properties, such as the amino acid sequence of the protein or molecular weight, which would allow for one to identify the protein without ambiguity. The mere recitation of a name does not adequately define the claimed protein. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed.

Claim 4 is vague and confusing due to the semicolon after the phrase ‘consisting of’ and then a colon prior to “a)". Additionally, it is unclear what structure is encompassed by the ‘injection domain of a Rho Gtpase activator’ and

the ‘catalytic domain of Rho Gtpase activator’. Claim 1, from which claim 4 depends, recites no sequence. The mere recitation of a name to describe the invention is not sufficient to satisfy the Statute's requirement of adequately describing and setting forth the inventive concept. The claim should provide any structural properties, such as the amino acid sequence of the protein or molecular weight, which would allow for one to identify the protein without ambiguity. The mere recitation of a name does not adequately define the claimed protein. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed.

Claim 11 is vague and confusing due to the semicolon after the phrase ‘consisting of’ and then a colon prior to “a)". Claim 11 is also vague and confusing because it is unclear if the ‘protein’ is different from the ‘immunoadjuvant’ as it also comprises injection and catalytic domains. It is unclear how this claim is different from claim 4. It seems to be reciting 'a polypeptide located within a larger protein, but still reads on the 'protein'. The wording is extremely vague and confusing. Appropriate correction is required.

Claim 11 is vague and indefinite because it is unclear if it is claiming solely the proteins (which were well known in the prior art; see 102(b) rejections below) or the vaccine compositions from which it depends. The wording of the claims

make it difficult to ascertain. If it is the former, then the claim should specify that the proteins have been isolated.

Claims 15 and 16 are vague and indefinite because they are drawn to methods for 'preparing a comprising'. Claim 15 also recites the limitation "the polypeptide. There is insufficient antecedent basis for this limitation in the claim. Claim 1 from which it depends does not recite a polypeptide.

Claim 16 is vague and indefinite due to the phrase 'adding the polypeptide according to claim 11' because claim 11 recites a protein comprising a polypeptide. Does claim 16 intend for the embedded polypeptide to be used or the protein comprising the polypeptide? Appropriate correction is required.

Claim Objections

2. Claims 2, 3, 5, 6 and 14 are objected to because of the following informalities:

Claims 2, 5, 6 and 14 contain dashes in the claim which do not belong. It is unclear what the dashes following the commas are representing.

Claims 2, 3, 5, 6 and 14 contain sequence identification numbers. However, the claims are not consistent with the use of the abbreviation for SEQ ID No., in some instances 'SEQID N$^{0'}$ is used while other times 'SEQ ID N$^{0'}$ is used. It is suggested that the claims recite 'SEQ ID NO.'

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-6, 9-11 and 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by any one of Felmlee et al **(**J. Bacteriol. 163:94-105(1985), Falbo et al Infect Immun. 1993. 61: 4909-4914), or Buetow et al Nat. Struct. Biol. 2001. 8:584-588)**.**

Femlee et al teach the nucleotide sequence of an E.coli chromosomal hemolysin and the polypeptide it encodes. Falbo teach the isolation and nucleotide sequence of the gene encoding cytoxic necrotizing factor 1 of E.coli. Buetow et al teach the structure of the Rho-activating domain of E.coli cytotoxic necrotizing factor 1. All of the references teach that their sequences are 100% identical to Applicant's SEQ ID NO: 1 and, therefore, inherently comprise the amino acid sequence starting at residue 720 and ending at residue 1014 of Applicant's SEQ ID NO: 1. See sequence alignment in Public PAIR (under 'Score/Suppl.content tab). The claimed vaccine composition comprises solely an immunoadjuvant compound which consists of a Rho Gtpase activator. The term "vaccine" is an intended use only. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior

art. If the prior art structure is capable of performing the intended use, then it meets the claim. An 'excipient' reads on water and therefore would be inherent in the preparation of the polypeptides.

4. Claims 1-6, 9-11 and 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Oswald et al (Proc. Natl. Acad. Sci. USA 1994. 91: 3814-3818).

Oswald et al teach a cytotoxic necrotizing factor type 2 protein produced by virulent E.coli and teach that it modifies the small GTP-binding protein Rho involved in assembly of actin stress fibers. The protein possess an amino acid sequence which is 100% identical to Applicant's SEQ ID NO: 2 and; therefore, would inherently comprise residue 720-1020. See sequence alignment in Public PAIR (under 'Score/Suppl.content tab). The claimed vaccine composition comprises solely an immunoadjuvant compound which consists of a Rho Gtpase activator. The term "vaccine" is an intended use only. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. An 'excipient' reads on water and therefore would be inherent in the preparation of the polypeptide.

5. Claims 1-6, 9-11 and 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Lockman et al (Infect. Immun. 2022. 70: 2708-2714).

Lockman et al teach a cytotoxic necrotizing factor produced by Yersinia pseudotuberculosis. The protein possess an amino acid sequence which is 100% identical to Applicant's SEQ ID NO: 3 and; therefore, would inherently

comprise residue 720-1014. See sequence alignment in Public PAIR (under 'Score/Suppl.content tab).The claimed vaccine composition comprises solely an immunoadjuvant compound which consists of a Rho Gtpase activator. The term "vaccine" is an intended use only. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. An 'excipient' reads on water and therefore would be inherent in the preparation of the polypeptide.

6. Claims 1-6, 9-11 and 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by any one Walker et al (Infect. Immun. 62: 3817-3828), Sharp et al (Nat.Genet. 2003. 35: 32-40), or Pullinger et al (Infect. Immun. 1996. 64: 4163-4171).

Walker et al teach the dermonectrotic toxin from the Genus Bordetella. Sharp et al teach the dermonectrotic toxin from several species of Bordetella. Pullinger et al teach the cloning, expression and molecular characterization of the dermonecrotic toxin gene of Bordetella spp. All of the references teach that their sequences are 100% identical to Applicant's SEQ ID NO: 4 and, therefore, inherently comprise the amino acid sequence starting at residue 1146 and ending at residue 1451 of Applicant's SEQ ID NO: 4. See sequence alignment in Public PAIR (under 'Score/Suppl.content tab).The claimed vaccine composition comprises solely an immunoadjuvant compound which consists of a Rho Gtpase activator. The term "vaccine" is an intended use only. A recitation of the

intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. An 'excipient' reads on water and therefore would be inherent in the preparation of the polypeptides.

7. Claims 1-6, 9-11 and 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by any one of Mirold et al (2001. J. Mol. Biol. 2001. 312: 7-16), Mirold et al. (Proc. Natl. Acad. Sci. USA. 1999. 96: 9845-9850), and Parkhill et al. (Nature. 2001. 413: 848-852).

Mirold et al (2001) teach the Salmonella type III effector sopE which is an activator for both CDC42 and RAC1 , e.g., a Rho Gtpases activator. Mirold et al (1999) teach the isolation of a temperate bacteriophage encoding the Salmonella type III effector sopE from an epidemic S.typhimurium strain. Parkhill etal teach the sequence of the sopE from S.enterica serovar Typhi CT 18. All of the references teach that their sequences are 100% identical to Applicant's SEQ ID NO: 5. See sequence alignment in Public PAIR (under 'Score/Suppl.content tab).The claimed vaccine composition comprises solely an immunoadjuvant compound which consists of a Rho Gtpase activator. The term "vaccine" is an intended use only. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the

claim. An 'excipient' reads on water and therefore would be inherent in the preparation of the polypeptides.

8. Claims 1-6, 9-11 and 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by any one of Bakshi et al (J.bacteriol. 2000. 182: 2341-2344), Stender et al (Mol.Microbiol. 2000. 36: 1206-1221), McClelland et al. 2001. Nature 413: 852-856), and Ehrbar et al (J.Baceteriol. 2003. 185: 6950-6967).

Bakshi et al teach the identification of SopE2, from Salmonella which is highly homologous to SopE and involved in the invasion of epithelial cells. Stender et al teach the identification of SopE2, from Salmonella typhimurium. McClelland et al teach the identification of SopE2, from Salmonella typhimurium. Ehrbar et al teach the role of the Salmonella pathogenicity island 1 (SPI-1) protein InvB in type III secretion of SopE and SopE2, two Salmonella effector proteins encoded outside of SPI-1 All of the references teach that their sequences are 100% identical to Applicant's SEQ ID NO: 6. See sequence alignment in Public PAIR (under 'Score/Suppl.content tab).The claimed vaccine composition comprises solely an immunoadjuvant compound which consists of a Rho Gtpase activator. The term "vaccine" is an intended use only. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. An 'excipient' reads on water and therefore would be inherent in the preparation of the polypeptides.

9. Claims 1-6, 9-11 and 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Lan et al (Infect. Immun. 2003. 71: 6298-6306).

Lan etal teach the polypeptide ipaC from Shigella. The reference teaches that their sequence is 100% identical to Applicant's SEQ ID NO: 7. See sequence alignment in Public PAIR (under 'Score/Suppl.content tab). The claimed vaccine composition comprises solely an immunoadjuvant compound which consists of a Rho Gtpase activator. The term "vaccine" is an intended use only. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. An 'excipient' reads on water and therefore would be inherent in the preparation of the polypeptides.

10. Claims 1-6, 9-11 and 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Smith et al (Nature. 1997. 388: 539-547).

Smith et al teach the Gtpase activator, cagA, from Helicobator pylori. The reference teaches that their sequence is 100% identical to Applicant's SEQ ID NO: 8. See sequence alignment in Public PAIR (under 'Score/Suppl.content tab). The claimed vaccine composition comprises solely an immunoadjuvant compound which consists of a Rho Gtpase activator. The term "vaccine" is an intended use only. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the

prior art structure is capable of performing the intended use, then it meets the claim. An 'excipient' reads on water and therefore would be inherent in the preparation of the polypeptides.

11. Claims 1-6, 9-11 and 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by any one of Ron et al (EMBO J. 1988. 7: 2465-2473), Komai et al (Bichem. Biophys. Res. Commun.2002. 299: 455-458), Eva et al. (Proc, Natl. Acad. Sci USA 1988. 85: 2061-2065), Shunichi et al (US 6,660,847).

Ron et al teach the polypeptide human dbl. Komai et al teach variants of the human DBL (MCF-2). Eva et al teach the DBL oncogene product, a distinct class of transforming protein. Shunichi et al teach the polypeptide DBL.The references all teach that their sequences are 100% identical to Applicant's SEQ ID NO: 9. See sequence alignment in Public PAIR (under 'Score/Suppl.content tab). The claimed vaccine composition comprises solely an immunoadjuvant compound which consists of a Rho Gtpase activator. The term "vaccine" is an intended use only. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. An 'excipient' reads on water and therefore would be inherent in the preparation of the polypeptides.

Claim Rejections - 35 USC § 112-Enablement

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1-11 and 14-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

Instant claims 1, 4, 7-11, 15 and 16 are broadly drawn to a vaccine comprising an immunoadjuvant compound which consists of ***any*** Rho GTPase activator and methods for preparing compositions comprising them by adding an excipient. Claims 7 and 8 allow for the addition of an antigen and claims 2, 5, 6 and 14 recite the polypeptide sequences of specific Rho GTPase activators.

The instant specification does not enable the use of any Rho Gtpase as an immunoadjuvant in a vaccine composition. The structure of Rho Gtpase and their sources vary greatly. It is unclear that they possess a mutual level of adjuvant-like activity. The instant specification has shown unexpected results with the use of cytotoxic necrotizing factor 1 (cnf1) (SEQ ID NO: 2) as an immunoadjuvant and have demonstrated that when the catalytic domain of cnf1

is present and active the polypeptide works to effectively boost the immune response to OVA. It was shown that a catalytically inactive CNF1 mutant did not possess the same adjuvant activity. The specification also has provided a smaller scale example of some success with the use of dermonectrotic toxin (DNT) (SEQ ID NO: 4). However, there are no other examples demonstrating immunoadjuvant activity of any other Rho Gtpase activator. While Applicants need not disclose every single species of a Genus or show working examples for every possible species, a representative number of examples should be shown. Given the great diversity and source of a 'Rho Gtpase' as defined by the instant specification, the examples provided with cnf1 and DNT are insufficient to enable the broad scope of the invention. Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 clearly states: "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." Additionally, the claims are drawn to 'vaccine compositions' and encompass vaccines drawn to protecting against HIV viruses (see claim 8). There is no known working vaccine

to prevent against HIV. Accordingly, one skilled in the art could not use any HIV antigen and any Rho Gtpase activator and come up with an effective vaccine composition against AIDS without undue experimentation.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

14. Claim 11 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim reads on a product of nature and should recite that the protein has been "isolated". As stated in the 112, second paragraph rejection above, it is unclear whether this claim is drawn to solely the known proteins or to a 'vaccine composition' as recited in preceding claim 4.

Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is 571-273-8300 which is able to receive transmissions 24 hours/day, 7 days/week.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571) 272-0858. The examiner can normally be reached on Monday-Thursday from 8:00 AM-6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi, can be reached on (571) 272-0956.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.

/Jennifer E. Graser/
Primary Examiner, Art Unit 1645

1/4/09